Supplemental Material

Table S1. Patients at higher risk for cardiovascular toxicity according to the recent guidelines.

Guidelines	High-risk patients
ESC-2016	▪ High doses of anthracyclines ▪ Female sex ▪ >65 years old or <18 years old ▪ Renal failure ▪ Concomitant or previous radiotherapy involving the heart ▪ Combination chemotherapy with both type I and type II agents ▪ Established or risk factors for cardiovascular disease ▪ Genetic factors
ASCO-2017	▪ High-dose anthracycline (eg, doxorubicin ≥250 mg/m^2, epirubicin ≥600 mg/m^2) ▪ High-dose radiotherapy (≥30 Gy) where the heart is in the treatment field ▪ Lower-dose anthracycline (eg, doxorubicin <250mg/m^2, epirubicin <600mg/m^2) in combination with lower-dose RT (<30 Gy) ▪ Treatment with lower-dose anthracycline (doxorubicin <250 mg/m^2, epirubicin <600 mg/m^2) or trastuzumab alone, and presence of any of the following risk factors: o Multiple cardiovascular risk factors (≥ two risk factors), including smoking, hypertension, diabetes, dyslipidemia, and obesity, during or after completion of therapy o Older age (≥ 60 years old) at cancer treatment o Compromised cardiac function (eg, borderline low LVEF [50% to 55%], history of myocardial infarction, ≥ moderate valvular heart disease) at any time before or during treatment ▪ Treatment with lower-dose anthracycline (eg, doxorubicin <250 mg/m^2, epirubicin <600 mg/m^2) followed by trastuzumab (sequential therapy)
ESMO-2020	▪ Prior anthracycline-based treatment ▪ >75 years old or <10 years old ▪ Prior mediastinal or chest radiotherapy ▪ Hypertension (before or at the time of treatment) ▪ Smoking exposure (current or previous) ▪ Previous combined treatment with trastuzumab and an anthracycline ▪ Elevated cardiac biomarkers before initiation of anticancer therapy ▪ Baseline abnormal systolic left ventricular function with LVEF <50% ▪ Pre-existing diabetes mellitus

LVD=left ventricular dysfunction; LVEF=left ventricular ejection fraction

Table S2. Baseline evaluation, monitoring and primary prevention in patients treated with anthracyclines according to the current guidelines.

Guidelines	Before cancer treatment	During cancer treatment	After cancer treatment
ESC-2016	▪ **Baseline evaluation** o Clinical*, ECG, TTE† with GLS. o Troponins, BNP or NT pro-BNP may be considered. o CMR is recommended if the quality of TTE is sub-optimal. ▪ **Primary prevention** o Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits. o If HF or significant LVD the patient should be discussed with the oncology team and options for non-anthracycline–containing chemotherapy and/or cardioprotection should be considered. o If baseline cardiotoxicity risk is high due to pre-existing cardiovascular disease, previous anthracycline-containing chemotherapy or poorly controlled cardiovascular risk factors, anthracyclines dose (>250–300 mg/m^2 doxorubicin or equivalent), a prophylactic cardioprotective medication regimen should be considered.	▪ **Monitoring** o TTE† with GLS should be performed at the end of the treatment in all patients. o For higher-dose anthracycline-containing regimens and in patients with high baseline risk, earlier assessment of cardiac function after a cumulative total doxorubicin or equivalent dose of 240 mg/m^2 should be considered. o Troponins may be used at each cycle of anthracyclines. ▪ **Primary prevention** o Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits. o Dexrazoxane can be considered in adults with advanced or metastatic breast cancer who have received a cumulative dose of >300 mg/m^2 doxorubicin or >540 mg/m^2 epirubicin and would benefit from continued anthracycline-based therapy.	▪ **Monitoring** o Clinical*, ECG, TTE† with GLS at 1 and 5 years after completion of cancer treatment in survivors who have completed higher-dose anthracycline-containing chemotherapy (≥300 mg/m^2 of doxorubicin or equivalent) or who developed cardiotoxicity requiring treatment. o Clinical*, ECG, TTE† with GLS in elderly patients and in patients with risk factors for cardiotoxicity. o Periodic screening with cardiac imaging and biomarkers, such as BNP, should be considered in survivors, particularly those treated with high cumulative doses or who demonstrated reversible LVD during cancer treatment. ▪ **Primary prevention** Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits.
ASCO-2017	▪ **Baseline evaluation** Clinical*, ECG, TTE† with GLS. ▪ **Primary prevention** Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits.	▪ **Monitoring** o Clinical*, ECG o In patients with clinical signs or symptoms of HF the following strategy is recommended: - TTE† with GLS, CMR or MUGA scan if TTE is not available or technically feasible, with preference given to CMR. - Troponin, BNP or NT pro-BNP. - Referral to a cardiologist. o Routine surveillance imaging (including TTE† with GLS) may be offered during treatment in asymptomatic patients considered to be at increased risk of developing LVD‡. Frequency of surveillance should be determined by health care providers. ▪ **Primary prevention** o Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits.	▪ **Monitoring** o Clinical*, ECG o In patients with clinical signs or symptoms of HF the following strategy is recommended: - TTE with GLS, CMR or MUGA scan if TTE is not available or technically feasible, with preference given to CMR. - Troponin, BNP or NT pro-BNP. - Referral to a cardiologist. o TTE† with GLS may be performed between 6 and 12 months after completion of cancer therapy in asymptomatic patients considered to be at increased risk of LVD‡. o CMR or MUGA scan may be offered if an TTE is not available or technically feasible, with preference given to CMR. o No recommendations can be made regarding the frequency and duration of surveillance in patients at increased risk‡

		○ Cardioprotection strategies may be incorporated, including use of dexrazoxane, continuous infusion, or liposomal formulation of doxorubicin, in patients planning to receive high-dose anthracyclines (doxorubicin ≥250 mg/m^2, epirubicin ≥600 mg/m^2).	who are asymptomatic and have no evidence of LVD on their 6- to 12-month post-treatment TTE. ▪ **Primary prevention** Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits.
ESMO-2020	▪ **Baseline evaluation** ○ Clinical*, ECG, TTE† with GLS measurement. ○ Troponins, BNP or NT pro-BNP should be considered in high-risk patients (with pre- existing significant cardiovascular disease) and those receiving high doses of anthracyclines. ▪ **Primary prevention** ○ Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits. ○ In patients with LVEF <50% but ≥40%, medical therapy with an ACE$_i$, ARB and/ or BB is recommended before treatment. ○ In patients with LVEF <40%, anthracycline therapy is not recommended unless there are no effective alternative anticancer treatment options. ○ In patients with a normal LVEF and cardiovascular risk factors particularly those exposed to multiple cardiotoxic agents, prophylactic use of ACE$_i$ or ARB (if intolerant to ACE$_i$) and/or selected BBs may be considered.	▪ **Monitoring** ○ In patients with clinical signs or symptoms of HF, cardiology consultation with reassessment of LVEF and potentially measuring cardiac biomarkers is recommended. ○ In asymptomatic patients with normal LVEF the following strategy is recommended: - Troponins, BNP or NT pro-BNP measurement (every 3-6 weeks or before each cycle), using the same institutional laboratory. - TTE[b] with GLS is recommended after a cumulative dose of doxorubicin 250 mg/m^2 or its equivalent anthracycline, after approximately each additional 100 mg/m^2 (or approximately epirubicin 200 mg/m^2) beyond 250 mg/m^2 and at the end of therapy, even if <400 mg/m^2. ▪ **Primary prevention** ○ Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits. ○ Dexrazoxane has been validated in selected populations who are receiving >300 mg/m^2 doxorubucin or equivalent. ○ Dexrazoxane can be considered regardless of the type of cancer, in patients with pre-existing cardiomyopathy, who require anthracyclines.	▪ **Monitoring** In asymptomatic patients with normal cardiac function, periodic consultation, ECG, TTE† with GLS should be considered at 6-12 months, at 2 years post-treatment and possibly periodically thereafter. ▪ **Primary prevention** Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits.

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* Including cardiological consultation with screening of cardiovascular diseases and risk factors.
† Including LVEF measurement (ideally 3D).
‡ Including:

- High-dose anthracycline (eg, doxorubicin ≥250 mg/m^2, epirubicin ≥600 mg/m^2)
- High-dose radiotherapy (≥30 Gy) where the heart is in the treatment field
- Lower-dose anthracycline (eg, doxorubicin <250mg/m^2, epirubicin <600mg/m^2) in combination with lower-dose RT (<30 Gy)
- Treatment with lower-dose anthracycline (doxorubicin <250 mg/m^2, epirubicin <600 mg/m^2) or trastuzumab alone, and presence of any of the following risk factors:

- Multiple cardiovascular risk factors (≥ two risk factors), including smoking, hypertension, diabetes, dyslipidemia, and obesity, during or after completion of therapy
- Older age (≥ 60 years old) at cancer treatment
- Compromised cardiac function (eg, borderline low LVEF [50% to 55%], history of myocardial infarction, ≥ moderate valvular heart disease) at any time before or during treatment

- Treatment with lower-dose anthracycline (eg, doxorubicin <250 mg/m^2, epirubicin <600 mg/m^2) followed by trastuzumab (sequential therapy)

ACE$_i$=angiotensin-converting-enzyme inhibitor; ARB=angiotensin receptor blocker; BB=betablocker; CMR=cardiac magnetic resonance; DTI=Doppler tissue imaging; GLS=global longitudinal strain; HF=heart failure; LLN=low limit of normal; LV=left ventricle; LVD=left ventricular dysfunction; LVEF=left ventricular ejection fraction; MUGA=multigated acquisition; TTE=transthoracic echocardiogram

Table S3. Baseline evaluation, monitoring and primary prevention in patients treated with HER2 inhibitors according to the current guidelines.

Guidelines	Before cancer treatment	During cancer treatment	After cancer treatment
ESC-2016	▪ **Baseline evaluation** o Clinical*, ECG, TTE† with GLS. o Troponins, BNP or NT pro-BNP may be considered. o CMR is recommended if the quality of TTE is sub-optimal. ▪ **Primary prevention** o Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits. o If HF or significant LVD the patient should be discussed with the oncology team and options for cardioprotection should be considered. o If baseline cardiotoxicity risk is high due to pre-existing cardiovascular disease, previous anthracycline-containing chemotherapy or poorly controlled cardiovascular risk factors, anthracyclines dose (>250–300 mg/m^2 doxorubicin or equivalent), a prophylactic cardioprotective medication regimen should be considered.	▪ **Monitoring** o For low-risk patients (normal baseline echocardiogram, no clinical risk factors), surveillance should be considered with TTE† every 4 cycles of anti-HER2 treatment. o Troponin with every cycle may be considered in patients with high baseline risk. o More frequent surveillance may be considered for patients with abnormal baseline echocardiography (e.g. reduced or low normal LVEF, structural heart disease) and those with higher baseline clinical risk (e.g. prior anthracyclines, previous myocardial infarction, treated HF) o TTE† with GLS should be performed at the end of the treatment in all patients. ▪ **Primary prevention** Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits.	▪ **Monitoring** o Clinical*, ECG, TTE† with GLS in elderly patients and in patients with risk factors for cardiotoxicity. o Periodic screening with cardiac imaging and biomarkers, such as BNP, should be considered in survivors, particularly those treated with high cumulative doses of anthracyclines or who demonstrated reversible LVD during cancer treatment. ▪ **Primary prevention** Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits.
ASCO-2017	▪ **Baseline evaluation** Clinical*, ECG, TTE† with GLS. ▪ **Primary prevention** Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits.	▪ **Monitoring** o Clinical*, ECG o In patients with clinical signs or symptoms of HF the following strategy is recommended: - TTE† with GLS, CMR or MUGA scan if TTE is not available or technically feasible, with preference given to CMR. - Troponin, BNP or NT pro-BNP. - Referral to a cardiologist. o Routine surveillance imaging (including TTE[b] with GLS) may be offered during treatment in asymptomatic patients considered to be at increased risk of developing LVD‡. Frequency of surveillance should be determined by health care providers. ▪ **Primary prevention**	▪ **Monitoring** o Clinical*, ECG o In patients with clinical signs or symptoms of HF the following strategy is recommended: - TTE† with GLS, CMR or MUGA scan if TTE is not available or technically feasible, with preference given to CMR. - Troponin, BNP or NT pro-BNP. - Referral to a cardiologist. o TTE† with GLS may be performed between 6 and 12 months after completion of cancer therapy in asymptomatic patients considered to be at increased risk of LVD‡. o CMR or MUGA scan may be offered if an TTE is not available or technically feasible, with preference given to CMR.

		Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits.	○ No recommendations can be made regarding the frequency and duration of surveillance in patients at increased risk who are asymptomatic and have no evidence of LVD on their 6- to 12-month post-treatment TTE. ▪ **Primary prevention** Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits.
ESMO-2020	▪ **Baseline evaluation** ○ Clinical*, ECG, TTE† with GLS measurement. ○ Troponins, BNP or NT pro-BNP should be considered in high-risk patients (with pre-existing significant cardiovascular disease) and those receiving high doses of anthracyclines. ▪ **Primary prevention** ○ Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits. ○ In patients with LVEF <50% but ≥40%, medical therapy with an ACE_i, ARB and/ or BB is recommended before treatment. ○ In patients with a normal LVEF and cardiovascular risk factors particularly those exposed to multiple cardiotoxic agents, prophylactic use of ACE_i or ARB (if intolerant to ACE_i) and/or selected BBs may be considered.	▪ **Monitoring** ○ In patients with clinical signs or symptoms of HF, cardiology consultation with reassessment of LVEF and potentially measuring cardiac biomarkers is recommended. ○ In asymptomatic non-metastatic patients undergoing adjuvant trastuzumab treatment, routine surveillance consisting of cardiac imaging every 3 months should be considered. ○ In asymptomatic patients undergoing anti-HER2-based treatment of metastatic disease, surveillance for CV toxicity that may consist of periodic cardiac physical examination, cardiac biomarkers and/or cardiac imaging should be considered. ○ Cardiac biomarker assessment may be considered as a valuable tool for cardiac safety surveillance in patients receiving adjuvant anti-HER2-based treatment. ▪ **Primary prevention** Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits.	▪ **Monitoring** For asymptomatic patients with normal cardiac function, periodic consultation, ECG, TTE† with GLS should be considered at 6-12 months, at 2 years post-treatment and possibly periodically thereafter. ▪ **Primary prevention** Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits.

* Including cardiological consultation with screening of cardiovascular diseases and risk factors.
† Including LVEF measurement (ideally 3D).
‡ Including:
- High-dose anthracycline (eg, doxorubicin ≥250 mg/m^2, epirubicin ≥600 mg/m^2)
- High-dose radiotherapy (≥30 Gy) where the heart is in the treatment field
- Lower-dose anthracycline (eg, doxorubicin <250mg/m^2, epirubicin <600mg/m^2) in combination with lower-dose RT (<30 Gy)
- Treatment with lower-dose anthracycline (doxorubicin <250 mg/m^2, epirubicin <600 mg/m^2) or trastuzumab alone, and presence of any of the following risk factors:
  - Multiple cardiovascular risk factors (≥ two risk factors), including smoking, hypertension, diabetes, dyslipidemia, and obesity, during or after completion of therapy
  - Older age (≥ 60 years old) at cancer treatment

- Compromised cardiac function (eg, borderline low LVEF [50% to 55%], history of myocardial infarction, ≥ moderate valvular heart disease) at any time before or during treatment
- Treatment with lower-dose anthracycline (eg, doxorubicin <250 mg/m^2, epirubicin <600 mg/m^2) followed by trastuzumab (sequential therapy)

ACE$_i$=angiotensin-converting-enzyme inhibitor; ARB=angiotensin receptor blocker; BB=betablocker; CMR=cardiac magnetic resonance; DTI=Doppler tissue imaging; GLS=global longitudinal strain; HF=heart failure; LLN=low limit of normal; LV=left ventricle; LVD=left ventricular dysfunction; LVEF=left ventricular ejection fraction; MUGA=multigated acquisition; TTE=transthoracic echocardiogram

Table S4. Baseline evaluation, monitoring and primary prevention in patients treated with VEGF inhibitors, Bcr-Abl kinase inhibitors, and proteasome inhibitors according to the current guidelines.

Guidelines	Before cancer treatment	During cancer treatment	After cancer treatment
ESC-2016	▪ **Baseline evaluation** Clinical*, ECG, TTE† with GLS. ▪ **Primary prevention** o Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits. o If baseline cardiotoxicity risk is high due to pre-existing cardiovascular disease, previous anthracycline-containing chemotherapy or poorly controlled cardiovascular risk factors, anthracyclines dose (>250–300 mg/m^2 doxorubicin or equivalent), a prophylactic cardioprotective medication regimen should be considered.	▪ **Monitoring** o Clinical evaluation in the first 2–4 weeks after starting $VEGF_i$ if baseline risk is high. o Consider periodic TTE, for example, every 6 months during $VEGF_i$ therapy. ▪ **Primary prevention** o Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits. o If baseline cardiotoxicity risk is high due to pre-existing cardiovascular disease, previous anthracycline-containing chemotherapy or poorly controlled cardiovascular risk factors, anthracyclines dose (>250–300 mg/m^2 doxorubicin or equivalent), a prophylactic cardioprotective medication regimen should be considered.	▪ **Monitoring** o Clinical*, ECG, TTE† with GLS in elderly patients and in patients with risk factors for cardiotoxicity. o Periodic screening with cardiac imaging and biomarkers, such as BNP, should be considered in survivors, particularly those who demonstrated reversible LVD during cancer treatment. ▪ **Primary prevention** Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits.
ASCO-2017	▪ **Baseline evaluation** Clinical*, ECG, TTE† with GLS. ▪ **Primary prevention** Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits.	▪ **Monitoring** o Clinical*, ECG o In patients with clinical signs or symptoms of HF the following strategy is recommended: - TTE[b] with GLS, CMR or MUGA scan if TTE is not available or technically feasible, with preference given to CMR. - Troponin, BNP or NT pro-BNP. - Referral to a cardiologist. ▪ **Primary prevention** Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits.	▪ **Monitoring** o Clinical*, ECG o In patients with clinical signs or symptoms of HF the following strategy is recommended: - TTE with GLS, CMR or MUGA scan if TTE is not available or technically feasible, with preference given to CMR. - Troponin, BNP or NT pro-BNP. - Referral to a cardiologist. ▪ **Primary prevention** Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits.
ESMO-2020	▪ **Baseline evaluation** o Clinical*, ECG, TTE† with GLS measurement. o Establishment of a baseline blood pressure measurement. o Troponins, BNP or NT pro-BNP should be considered in high-risk patients (with pre-existing significant cardiovascular disease). ▪ **Primary prevention**	▪ **Monitoring** o Serial BP monitoring is recommended along with surveillance for the early detection of cardiovascular toxicity that may consist of periodic cardiac physical examination, cardiac biomarkers and/or cardiac imaging. o In patients with clinical signs or symptoms of HF, cardiology consultation with reassessment of LVEF and potentially measuring cardiac biomarkers is recommended.	▪ **Monitoring** For asymptomatic patients with normal cardiac function, periodic consultation, ECG, TTE† with GLS should be considered at 6-12 months, at 2 years post-treatment and possibly periodically thereafter. ▪ **Primary prevention**

	○ Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits. ○ In patients with LVEF <50% but ≥40%, medical therapy with an ACE_i, ARB and/ or BB is recommended before treatment. ○ Optimization of blood pressure control. ○ Avoid non-dihydropyridine calcium channel blockers (diltiazem and verapamil) are typically contraindicated, since they are inducers of cytochrome P450 3A4 (CYP3A4) resulting in increased VEGF signaling pathway inhibitors levels. ○ In patients with a normal LVEF and cardiovascular risk factors particularly those exposed to multiple cardiotoxic agents, prophylactic use of ACE_i or ARB (if intolerant to ACE_i) and/or selected BBs may be considered.	▪ **Primary prevention** ○ Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits. ○ Optimization of blood pressure control. ○ For patient with $VEGF_i$ therapy, avoid non-dihydropyridine calcium channel blockers (diltiazem and verapamil) because they are inhibitors of cytochrome P450 3A4 (CYP3A4) resulting in increased $VEGF_i$ levels.	Actively manage modifiable cardiovascular risk factors and diseases. Encourage to exercise on a regular basis and healthy dietary habits

* Including cardiological consultation with screening of cardiovascular diseases and risk factors.
† Including LVEF measurement (ideally 3D).
ACE_i=angiotensin-converting-enzyme inhibitor; ARB=angiotensin receptor blocker; BB=betablocker; BP=blood pressure; CMR=cardiac magnetic resonance; DTI=Doppler tissue imaging; GLS=global longitudinal strain; HF=heart failure; LLN=low limit of normal; LV=left ventricle; LVD=left ventricular dysfunction; LVEF=left ventricular ejection fraction; MUGA=multigated acquisition; TTE=transthoracic echocardiogram; $VEGF_i$; vascular-endothelium growth factor signaling pathway inhibitors.

Table S5. Baseline evaluation, monitoring and primary prevention in patients treated with immune checkpoint inhibitors according to the current guidelines.

Guidelines	Before cancer treatment	During cancer treatment	After cancer treatment
ESC-2016	No recommendations.	No recommendations.	No recommendations.
ASCO-2017	No recommendations.	No recommendations.	No recommendations.
ESMO-2020	No recommendations.	▪ For patients who develop new CV symptoms or are incidentally noted to have arrhythmia conduction abnormality on ECG or LVSD on echocardiogram, while undergoing of ICI therapy ▪ Further appropriate work-up ▪ ECG ▪ Troponin ▪ BNP or NT-pro BNP ▪ CRP ▪ Viral titer ▪ Echo with GLS ▪ CMR ▪ EMB for diagnosis should be considered if the diagnosis is highly suspected with otherwise negative work-up	No recommendations.
ESMO – specific for ICI toxicity-2017	No recommendations.	No recommendations.	No recommendations.
ASCO – specific for ICI toxicity-2018	▪ ECG ▪ Consider troponin, especially in patient treated with combination immune therapies	Upon signs/symptoms (consider cardiology consult): ▪ ECG ▪ Troponin ▪ BNP ▪ Echocardiogram ▪ Chest X-ray Additional testing guided by cardiology and may include: ▪ Stress test ▪ Cardiac catherization ▪ CMR	No recommendations.

CMR=cardiac magnetic resonance; CRP=c-reactive protein; GLS=global longitudinal strain; ICI=immune checkpoint inhibitor; LVSD=left ventricular systolic dysfunction;

Table S6. Diagnostic criteria and management of myocardial toxicity and heart failure according to the recent guidelines.

Guidelines	Diagnostic criteria	Management of CTRCD and "subclinical" myocardial toxicity
ESC-2016	▪ **Cancer therapeutics-related cardiac dysfunction** Absolute decrease in the LVEF of >10 percentage points, to a value <50% ▪ **"Subclinical" left ventricular dysfunction** o Relative decrease from baseline in the GLS of >15%* OR o Troponins elevation (as defined by the cut-offs specific to the assay platform used in the individual labs) from baseline and measured before and/or 24 hours after each chemotherapy cycle.	▪ **Cancer therapeutics-related cardiac dysfunction** o ACE_i (or ARB) in combination with BB are recommended. o HF therapy should be continued indefinitely unless normal systolic LV function remains stable after cessation of HF therapy and no further cancer therapy is planned. o In patients with trastuzumab-induced cardiac dysfunction, HF treatment can be stopped after normalization. ▪ **"Subclinical" left ventricular dysfunction** o In patients with decrease in LVEF >10 percentage points but to a value ≥50% should undergo repeated assessment of LVEF shortly after and during the duration of cancer treatment. o In patients with a troponin increase during treatment with high dose of anthracyclines, cardioprotection may be considered. o In patients with a GLS decrease, cancer treatment should not be stopped, interrupted or reduced.
ASCO-2017	**Cardiac dysfunction** No definition provided.	**Cardiac dysfunction** o Referral to a cardiologist or a health care provider with cardio-oncology expertise. o No recommendations can be made regarding continuation or discontinuation of cancer therapy in individuals with evidence of cardiac dysfunction. This decision, made by the oncologist, should be informed by close collaboration with a cardiologist, fully evaluating the clinical circumstances and considering the risks and benefits of continuation of therapy responsible for the cardiac dysfunction.
ESMO-2020	▪ **Anti-cancer therapy-related cardiac dysfunction** o Absolute decrease in the LVEF of >20 percentage points OR o Absolute decrease in the LVEF of ≥10 percentage points to a value of <50% OR o Absolute decrease in the LVEF to a value of <50%. ▪ **"Subclinical" cardiac dysfunction** o Absolute decrease from baseline in the GLS of ≥5% OR o Relative decrease from baseline in the GLS of ≥12% OR o Troponins elevation (as defined by the cut-offs specific to the assay platform used in the individual labs) from baseline.	▪ **Anti-cancer therapy-related cardiac dysfunction** o In asymptomatic patients undergoing treatment with anthracyclines, with an LVEF decrease of ≥10% from baseline to 50%, or a decrease in LVEF to ≥40% but <50%, the following evaluations are recommended: - Cardiology consultation (preferably a cardio-oncology specialist). - Consider initiation of cardioprotective treatments (ACEi, ARBs and/or BB), if not already prescribed. - A statin may be considered if concomitant coronary disease is present. - Consider BNP or NT-proBNP and troponins and a cardiac-focused physical exam after each dose of anthracycline. - Repeat LVEF assessment after alternate doses of anthracyclines. - If further anthracycline-based chemotherapy is planned, the benefit-risk assessment of continued anthracyclines use as well as options of non-anthracycline regimens should be discussed, and the use of dexrazoxane and/or liposomal doxorubicin should be considered. o In asymptomatic patients undergoing treatment with trastuzumab, with an LVEF decrease of ≥10% from baseline or a drop in LVEF to ≥40% but <50%, the following evaluations are recommended: - Cardiology consultation, preferably a cardio-oncology specialist. - Consider initiation of cardioprotective treatments (ACE_i, ARBs and/or BB), if not already prescribed. - Consider BNP or NT-proBNP and troponins monthly and periodic cardiac-focused physical exam. - If trastuzumab is stopped, repeat LVEF within 3-6weeks, and resume trastuzumab therapy if LVEF has normalized to >50%. - Trastuzumab therapy may be continued with mild asymptomatic reductions in LVEF. o In patients undergoing treatment with trastuzumab (or any HER2-targeted molecular therapy) with signs and symptoms of HF, or an asymptomatic patient with an LVEF <40%, the same assessments as those for an LVEF ≥40% are recommended. In addition, trastuzumab (or any HER2-based therapy) should be withheld until the cardiac status has stabilized. A discussion regarding the risks and benefits of continuation should be held with the multidisciplinary team and the patient.

		○ In patients in whom trastuzumab therapy (or any HER2-targeted molecular therapy) has been interrupted, whose LVEF is ≥40% and/or whose signs and symptoms of HF have resolved, resumption of trastuzumab therapy should be considered, supported by: - Continued medical therapy for HF and ongoing cardiology care. - Periodic cardiac biomarker assessments. - Periodic LVEF assessments during ongoing treatment. ○ In patients in whom trastuzumab therapy (or any HER2-targeted molecular therapy) has been interrupted, whose signs and symptoms of HF do not resolve and/or LVEF remains <40%, resumption of trastuzumab therapy may be considered if no alternative therapeutic option exists. The risk-benefit assessment of prognosis from cancer versus HF should be discussed with the multidisciplinary team and the patient. ○ In patients undergoing treatment with sunitinib (or other anti-VEGF-based therapy), who shows signs and symptoms of HF, assessment and optimization of blood pressure control is recommended and measurement of LVEF and/or cardiac biomarkers should be considered. In addition, sunitinib (or other anti-VEGF-based therapies) should be interrupted. The patient should be assessed to determine whether reinstituting those therapies is appropriate. ○ For patients who developed LVD or HF due to any anticancer therapies, cardiovascular care including medical treatment with ACE_i, ARB and/or BB and regular cardiology review (e.g. annual if asymptomatic) should be continued indefinitely, regardless of improvement in LVEF or symptoms. Any decision to withdraw HF-based therapy should only be done after a period of stability, no active cardiac risk factors and no further active anticancer therapy. ▪ **"Subclinical" cardiac dysfunction** ○ In asymptomatic patients undergoing treatment with any cardiotoxic anticancer therapy, with normal LVEF but a decrease in average GLS from baseline assessment (≥12% relative decrease or ≥5% absolute decrease), the following evaluations/treatments should be considered: - Consider initiation of cardioprotective treatments (ACE_i, ARBs and/or BB), if not already prescribed. - Repeat LVEF/GLS measurement every 3 months unless a cardiac physical exam is required or symptoms develop (if this occurs, LVEF/GLS should be repeated with suspected cardiac toxicity). - Life-saving chemotherapy should not be altered solely based on changes in GLS. ○ In asymptomatic patients undergoing treatment with cardiotoxic anticancer therapy and an elevation in cardiac troponin, the following measures should be considered: - Cardiology consultation, preferably a cardio-oncology specialist. - Consider LVEF and GLS assessment with TTE. - Appropriate evaluation to exclude ischemic heart disease as a comorbidity. - Consider initiation of cardioprotective treatments (ACE_i, ARB and/or BB), if not already prescribed. - Consider initiation of dexrazoxane in patients with anthracyclines. - Anticancer therapy may be continued without interruption if only mild elevations in cardiac biomarkers occur without significant LVD.

* This decrease should be confirmed by repeated imaging done after 2-3 weeks.

ACE_i=angiotensin-converting-enzyme inhibitor; ARB=angiotensin receptor blocker; BB=betablocker; CMR=cardiac magnetic resonance; CTRCD=cancer treatment-related cardiac dysfunction; GLS=global longitudinal strain; HF=heart failure; LV=left ventricle; LVD=left ventricular dysfunction; LVEF=left ventricular ejection fraction; TTE=transthoracic echocardiogram.

Table S7. Diagnostic criteria and management of cancer treatment-related hypertension according to current guidelines.

Guidelines	Definitions	Management of cancer treatment-related hypertension
ESC-2016	BP >140/90 mmHg.	▪ Baseline assessment of cardiovascular risk factors, BP monitoring and optimal management of hypertension. ▪ Search for other medications may also increase BP (e.g. steroids, non-steroidal anti-inflammatory drugs, erythropoietin). ▪ Ambulatory blood pressure measurement should be considered, and lifestyle modification encouraged. ▪ After the initiation of a cancer treatment that may increase BP, early detection and reactive management of BP elevations are necessary and early and aggressive pharmacological management is recommended to prevent the development of cardiovascular complications ▪ Hypertension should be adequately treated according to the current standing clinical practice guidelines (treatment target is <140/90 mmHg). ▪ ACE_i or ARBs, BB and dihydropyridine calcium channel blockers (amlodipine, felodipine) are the preferred antihypertensive drugs. Non-dihydropyridine calcium channel blockers should preferably be avoided due to the risk of drug-drug interactions. Diuretics have the risk of electrolyte depletion and consequent QT prolongation and, although they may be used, caution is advised. ▪ Dose reduction or discontinuation of cancer treatment can be considered if BP is not controlled. ▪ Once BP control is achieved, cancer treatment can be restarted to achieve maximum cancer efficacy.
ASCO-2017	No recommendations.	Aggressive monitoring and management of hypertension can significantly lower the incidence of cardiotoxicity.
ESMO-2020	No recommendations.	▪ Factors that can contribute to BP elevation need to be addressed: obstructive sleep apnea, excessive alcohol consumption, nonsteroidal anti-inflammatory drugs, adrenal steroid hormones, erythropoietin, oral contraceptive hormones and sympathomimetics. ▪ Once stable BPs are achieved, home BP monitoring or routine clinical evaluations, at least every 2-3 weeks, should be performed for the remainder of cancer treatment ▪ Hypertension should be adequately treated according to the 2017 ACC/AHA guidelines (treatment target is <130/80 mmHg). ▪ ACE_i or ARBs and dihydropyridine calcium channel blockers (amlodipine, nifedipine) are the preferred antihypertensive drugs. The non-dihydropyridine calcium channel blockers (diltiazem and verapamil) are typically contraindicated due to the risk of drug-drug interactions. ▪ Discontinuation or dose reduction of cancer treatment might become necessary to control hypertension in a certain subset of patients not responding to any of the outlined measures.

BP=blood pressure; ACE_i=angiotensin-converting enzyme inhibitor; ARB=angiotensin receptor blocker; BB=beta-blocker.

Table S8. Diagnostic criteria and management of cancer treatment-related QTc interval prolongation according to current guidelines.

Guidelines	Diagnostic criteria	Management of cancer treatment-related QTc interval prolongation
ESC-2016	▪ **Standardized formulas** o Bazett's QT/$\sqrt{RR}$ or Fridericia's QT/$\sqrt[3]{RR}$. o The comparative measurements during treatment should all utilize the same chosen method. ▪ **QTc interval prolongation** o QTc prolongation >500 ms *AND/OR* o ΔQTc (i.e. change from baseline) of >60 ms *AND/OR* o Ventricular arrhythmias occurrence	▪ **Cancer treatment must be temporarily interrupted.** ▪ **Correction of electrolyte abnormalities and cardiac risk factors.** ▪ **Cancer treatment may be rechallenge at a reduced dose once the QTc normalizes.**
ASCO-2017	No recommendations.	No recommendations.
ESMO-2020	No recommendations.	No recommendations.

Table S9. Management of cancer treatment-related atrial fibrillation according to current guidelines.

Guidelines	Rhythm *vs.* rate control	Thromboembolic prophylaxis
ESC-2016	▪ **Decision should be patient-based and symptom directed** ▪ **In case of rate control strategy, beta-blockers, digoxin or the non-dihydropyridine calcium channel blockers can be used**	▪ **Decision based on CHA_2DS_2-VASc and HAS-BLED scores** ▪ **Anticoagulation can generally be considered if CHA_2DS_2-VASc ≥2 and platelet count is >50 000/mm^3** ▪ **Anticoagulation options include LMWH (as a short- to intermediate-term measure), warfarin and DOAC**
ASCO-2017	No recommendations.	No recommendations.
ESMO-2020	No recommendations.	No recommendations.

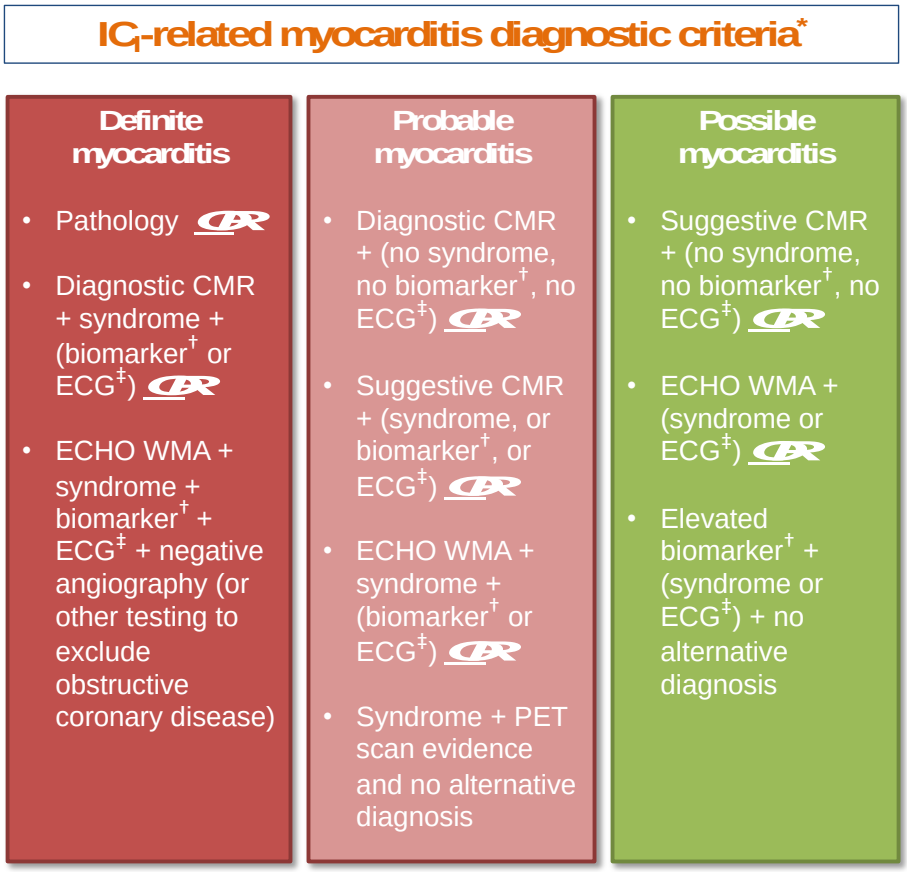
CHA_2DS_2VASc=congestive heart failure, hypertension, age ≥75, diabetes, stroke, vascular disease, age 65–74, and Sex (female); HAS-BLED=hypertension, abnormal, renal/liver function, stroke, bleeding history or predisposition, labile INR, elderly (>65years), drugs/alcohol; LMWH=low molecular weight heparin; DOAC= direct oral anti-coagulants.

Table S10. Diagnostic criteria and management of immune checkpoint inhibitor-related myocarditis according to the recent guidelines.

Guidelines	Diagnostic criteria	Management of immune checkpoint inhibitor-related myocarditis
ESC-2016	Not defined.	No recommendations.
ASCO-2017	Not defined.	No recommendations.
ESMO-2020	Not defined.	▪ For patients who develop new CV symptoms or are incidentally noted to have any arrhythmia, conduction abnormality on ECG or LVSD on echocardiogram, while undergoing (or after recent completion) of ICI therapy, further appropriate work-up (ECG, troponin, BNP or NT-pro-BNP, C-reactive protein, viral titer, echocardiogram with GLS, cardiac MRI) for ICI-associated CV toxicity, particularly myocarditis and other common differential diagnoses should be carried out promptly. ▪ Endomyocardial biopsy for diagnosis should be considered if the diagnosis is highly suspected with otherwise negative work-up. ▪ With either suspicion or confirmation of ICI-associated myocarditis, further therapy with ICIs should be withheld and high-dose corticosteroids (methylprednisolone 1000 mg/day followed by oral prednisone 1 mg/kg/day) should be initiated promptly. Corticosteroids should be continued until resolution of symptoms and normalization of troponin, LV systolic function and conduction abnormalities. ▪ For steroid-refractory or high-grade myocarditis with hemodynamic instability, other immunosuppressive therapies such as anti-thymocyte globulin, infliximab (except in patients with HF), mycophenolate mofetil or abatacept should be considered. ▪ For patients with cardiomyopathy and/or HF, appropriate guideline-directed medical therapy and hemodynamic support should be provided as indicated. ▪ For patients with atrial or ventricular tachyarrhythmia or heart block, appropriate medical and supportive care should be provided as indicated. ▪ ICI therapy should be permanently discontinued with any clinical myocarditis. The decision regarding restarting ICI therapy in the absence of alternative available antineoplastic therapy needs to be individualized with multidisciplinary discussion considering the cancer status, response to prior therapy, severity of cardiotoxicity, regression of toxicity with immunosuppressive therapy and patient preference after weighing the risks and benefits. If ICI therapy needs to be restarted, monotherapy with an anti-programmed cell death protein 1 (anti-PD-1) agent might be considered with very close surveillance for cardiotoxicity development.
ESMO – specific for ICI toxicity-2017	Not defined.	▪ Early consultation with a cardiologist. ▪ Admit the patient an immediately start high-dose (methyl) prednisone (1-2mg/kg). ▪ In case of deterioration, consider adding another immunosuppressive drug (mycophenolate mofetil or tacrolimus).
ASCO – specific for ICI toxicity-2018	Not defined.	▪ Hold ICI and permanently discontinue after grade 1. ▪ Administer high-dose corticosteroids (1 to 2 mg/kg of prednisone) initiated rapidly (oral or IV depending on symptoms). ▪ Admit patient and consult cardiology. ▪ Manage cardiac symptoms according to American College of Cardiology (ACC)/AHA guidelines and with guidance from cardiology. ▪ Offer immediate transfer to a coronary care unit for patients with elevated troponin or conduction abnormalities. ▪ In patients without an immediate response to high-dose corticosteroids, offer early institution of cardiac transplant rejection doses of corticosteroids (methylprednisolone 1 g every day) and the addition of either mycophenolate, infliximab, or antithymocyte globulin.

CV=cardiovascular; GLS=global longitudinal strain; HF=heart failure; ICI=immune checkpoint inhibitor; LV=left ventricle; LVSD=left ventricular systolic dysfunction; MRI=magnetic resonance imaging;

Figure S1. Myocarditis Definition.



† Troponin >99th percentile of the upper reference limit. Concomitant myositis may result in significant elevations of CK, CK isoforms, and even troponin T. In this scenario, troponin I would be the most specific option for myocardial injury. CK-MB should be used if troponin I is not available.

‡ ECG changes should be dynamic (change from baseline) in a timeframe consistent with the onset of the myocarditis syndrome. Possible changes are broad including arrhythmia, ST-T wave abnormalities, PR segment changes, or new arrhythmias (eg, new heart block or ectopy). ECG findings diagnostic for an alternative diagnosis (eg, regional ST segment elevation in the con- text of known acute coronary syndrome) should not be counted as changes consistent with myocarditis with- out appropriate investigation.

CMR=cardiac magnetic resonance; WMA=wall motion abnormality.

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